

REMARKS

I. Claim Status

Reconsideration of the present application is respectfully requested. Claims 1-5, 7-10, 12, 16, 19, 20, 22 and 33 are pending. Claims 6, 11, 13, 14, 15, 17, 18, 21, 23-32 and 34 have been previously canceled without prejudice.

II. Rejections Under 35 U.S.C. § 103(a)

A. U.S. Patent No. 3,257,276 to Broh-Kahn et al. in view of U.S. Patent No. 5,736,574 to Burnier et al. as evidenced by U.S. Patent No. 4,870,108 to Page

Claims 1, 16, 19 and 22 stand rejected under 35 U.S.C. § 103(a) as obvious over U.S. Patent No. 3,257,276 to Broh-Kahn et al. (hereafter, "Broh-Kahn") in view of U.S. Patent No. 5,736,574 to Burnier et al. (hereafter, "Burnier") as evidenced by U.S. Patent No. 4,870,108 to Page (hereafter, "Page"). The Examiner contends that Broh-Kahn describes an oral analgesic hydroalcoholic gel comprising benzalkonium chloride, a gelling agent, alcohol, and water among other ingredients. The Examiner further alleges that Burnier discloses antimicrobial mixtures comprising an antimicrobial agent and a synergistically effective amount of octoxyglycerin for formulating cosmetic and pharmacological compositions. According to the Examiner, it would have been obvious for an artisan of ordinary skill to combine Burnier's octoxyglycerin with the composition described by Broh-Kahn, which allegedly describes the claimed invention.

Applicants respectfully disagree. To support an assertion of obviousness, the Examiner must show that "all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination yielded nothing more than predictable results to one of ordinary skill in the art." M.P.E.P. § 2143. *See also KSR International Co. v. Teleflex Inc.*, 550 U.S. 398, 127 S.Ct. 1727 (2007).

The claims are not obvious over the combined teaching of the cited references because an artisan of ordinary skill would have no reasonable expectation that the compositions of Burnier and Broh-Kahn could be successfully combined into a single composition, as encompassed by the claims.

Broh-Kahn is directed to oral analgesic preparations for treating pain in the oral or buccal cavity. The formulations include a salicylate compound to treat the pain in the form of a hydroalcoholic gel. Broh-Kahn's hydroalcoholic gel is formulated for administration to the surface of the buccal mucosa and gingival tissue in the mouth, whereby the formulation is absorbed through the oral mucosa to provide a local analgesic effect while avoiding the side effects associated with systemically acting analgesic agents administered, for example, via ingestion. Broh-Kahn is able to achieve a local effect by formulating the hydroalcoholic gel with a sufficient viscosity to remain and act at the buccal mucosal surface, while avoiding ingestion through the swallowing of one's saliva. *See*, Broh-Kahn at Col. 3, lines 41-50; and Col. 3, line 73-Col. 4, line 11.

In preferred embodiments, Broh-Kahn discloses that a local analgesic effect at the oral mucosa can be achieved when the hydroalcoholic gel is formulated with methylcellulose-4000 at a concentration of 2.75%. *See*, Broh-Kahn at Col. 5, lines 15-25. As described by Broh-Kahn, methylcellulose-4000 (*i.e.*, "Methocel-4000"), has a viscosity of 4000 centipoises when formulated at a concentration of 2.0% in an aqueous solution that is maintained at 20°C. *See*, Broh-Kahn at Col. 4, lines 60-69. In contrast, the present claims recite that the claimed formulation has a viscosity below 2000 centipoises. Because Broh-Kahn discloses that its oral formulation must be sufficiently viscous to act locally at the oral mucosa, and further, that a composition formulated with 2.75% methylcellulose-4000 is sufficient for such a purpose, an artisan of ordinary skill would, at best, be motivated to formulate a composition for local administration to the oral cavity that has a viscosity of at least 4000 centipoises, as a less viscous formulation would be at risk for ingestion in one's saliva, which can lead to the systemic side effects that Broh-Kahn seeks to avoid.

Applicants also submit that the skilled artisan would have no reasonable expectation that the elements of the cited references could be successfully combined into a single composition because Broh-Kahn is directed to oral analgesic compositions, while Burnier is directed to topical antimicrobial cosmetic compositions. Nothing in Broh-Kahn suggests that its disclosed compounds, which are formulated for oral use, could be successfully adapted for use in a topical product, as described by Burnier. Similarly, Burnier does not suggest or describe that its topical formulations would be appropriate for use in the oral cavity, as described by Broh-Kahn. To the contrary, Burnier describes antimicrobial formulations to be used as an alternative to known

antimicrobial agents, such that an antimicrobial effect can be achieved while avoiding unpleasant side effects of prior art antimicrobials, such as irritation and allergic reactions. Additionally, the compositions of Burnier are formulated for use in the absence of alcohols or polyols, *e.g.*, ethanol or propylene glycol, as these can also cause irritation and allergic reactions when used at high concentrations. *See*, Burnier at Col. 1, lines 22-33. Thus, in view of Burnier, a skilled artisan would seek to combine octoxyglycerin with antimicrobial agents other than those known in the prior art, for example, as disclosed by Broh-Kahn, in an attempt to avoid unpleasant side effects. Furthermore, such compositions would be formulated in the absence of high concentrations of alcohol, for example, as described by Broh-Kahn (*see*, Broh-Kahn at Col. 5, lines 15-25 disclosing a composition comprising 39.16% ethyl alcohol), as the presence of alcohol in the formulation can also lead to unpleasant side effects.

Applicants further submit that a skilled artisan would have no reasonable expectation of success in practicing the claimed invention because Burnier does not suggest or describe that octoxyglycerin can be combined with any antimicrobial agents (*e.g.*, benzalkonium chloride as described in Broh-Kahn) other than hydrolipids and lipids.

. . . combinatory immixture of at least one compound exhibiting antimicrobial activity, *selected from among the hydrolipids or lipids*, and at least one glyceryl monoalkyl ether . . . The antimicrobial action of this combination is advantageous since it is milder, while at the same time being at least as effective as that of the compounds of the prior art . . .

See, Burnier at Col. 1, lines 41-50 (emphasis added). Thus, in view of Burnier, the skilled artisan would understand that octoxyglycerin could only be combined with a hydrolipid or a lipid to achieve an antimicrobial effect without causing the unpleasant side effects of prior art antimicrobials. Burnier does not suggest or describe that octoxyglycerin can be successfully combined with a quaternary ammonium compound, as recited by the claims, to have any effect.

Furthermore, with regard to the Examiner's contention that it would have been obvious to combine the various elements of the cited art, Applicants submit that while there are limited circumstances where an obviousness rejection may fairly be based on a contention that the invention was obvious to try, the instant rejection does not fall within those limited circumstances. As noted by the Supreme Court in *KSR v Teleflex*, 127 S.Ct. 1727, 1739 (2007),

it is inappropriate to employ an obvious to try argument in situations where the outcome cannot be reasonably predicted. *See, KSR v. Teleflex*, 127 S.Ct. 1727, 1739 (2007). This distinction between predictable situations where an obvious to try argument is appropriate and unpredictable situations where an obvious to try argument is an inappropriate basis for obviousness was recently clarified further by the Federal Circuit in *In re Kubin*, 561 F.3d 1531 (Fed. Cir. 2009):

In [unpredictable] circumstances, where a defendant merely throws metaphorical darts at a board filled with combinatorial prior art possibilities, courts should not succumb to hindsight claims of obviousness. The inverse of this proposition is succinctly encapsulated by the Supreme Court's statement in *KSR* that where a skilled artisan merely pursues "known options" from a "finite number of identified, predictable solutions," obviousness under § 103 arises.

In re Kubin, 561 F.3d 1531, 1359 (Fed. Cir. 2009).

In the present application, the claims are directed to a composition which exhibits antimicrobial synergy achieved by combining antimicrobially synergistic amounts of octoxyglycerin and a quaternary ammonium compound (e.g., benzalkonium chloride). For example, as disclosed in Example 4 of the specification (*see*, the specification at pages 38-42), octoxyglycerin produced a 33 fold reduction in microbial growth compared to control, and benzalkonium chloride produced a 6.25 fold reduction in microbial growth compared to control. However, when the two agents were combined together in a single composition, microbial growth was reduced by 12,500 fold compared to control. Such an effect is extraordinarily synergistic over the expected additive effect of the two agents (*i.e.*, 39.25 fold reduction). *See*, the specification at page 40, Table 5.

An artisan of ordinary skill, in view of the cited references, would have no way of predicting that octoxyglycerin and a quaternary ammonium compound would interact synergistically. Further, as discussed above, the skilled artisan would not only be unable to predict that the two agents could interact synergistically, but in view of the references, the skilled artisan would have no reasonable expectation that the two agents could even be combined together to have any effect. Specifically, without knowledge of the instant application, in which Applicants demonstrate that octoxyglycerin and a quaternary ammonium compound interact synergistically, the skilled artisan would not have expected or predicted that the two compounds could be combined to achieve such an effect.

For the foregoing reasons, Applicants submit that the claims are not obvious over the combined teaching of Broh-Kahn and Burnier, and respectfully request that the rejection be withdrawn.

B. U.S. Patent No. 3,257,276 to Broh-Kahn et al. in view of U.S. Patent No. 5,736,574 to Burnier et al. and U.S. Patent No. 4,393,076 to Noda et al. as evidenced by U.S. Patent No. 4,870,108 to Page

Claim 7 stands rejected under 35 U.S.C. § 103(a) as obvious over Broh-Kahn in view of Burnier and further in view of U.S. Patent No. 4,393,076 to Noda et al. (hereafter, "Noda") as evidenced by Page. The Examiner contends that Broh-Kahn describes a hydroalcoholic gel composition comprising benzalkonium chloride, a gelling agent, alcohol, and other ingredients, while Burnier discloses antimicrobial mixtures comprising an antimicrobial agent and synergistic amounts of octoxyglycerin, as previously discussed. The Examiner further alleges that Noda describes an anti-inflammatory and analgesic gel composition comprising methylcellulose or hydroxyethylcellulose. According to the Examiner, it would have been obvious to use Noda's methylcellulose or hydroxyethylcellulose in the composition described by Broh-Kahn and Burnier to produce the claimed invention.

Applicants respectfully disagree and submit that an artisan of ordinary skill would have no expectation that the methylcellulose or hydroxyethylcellulose of Noda could be successfully combined with the composition of Broh-Kahn, as contended by the Examiner. As previously discussed, Broh-Kahn discloses gel compositions for use in the oral or buccal cavity, whereby the composition is absorbed through the oral mucosa to provide a local analgesic effect. *See, e.g.,* Broh-Kahn at Col. 1, lines 10-27. In contrast, Noda is directed to gel compositions for external topical administration. *See, e.g.,* Noda at Col. 2, lines 40-51. Neither Broh-Kahn nor Noda provide the artisan with any guidance or suggestion that the ingredients for a topical composition as described by Noda could be combined with the ingredients of Broh-Kahn's oral composition to form an effective antimicrobial composition as encompassed by the claims. In particular, Noda recognizes that in general, ingredients from oral and topical formulations are not usually compatible:

It is seen from the foregoing that, in general, medicinal ingredients which are effective when orally administered are not necessarily effective when used as a gel composition for external application

to integument and, therefore, they must be intensively studied to find their uses...

See, Noda at Col. 2, lines 52-57. Thus, in view of Noda, the skilled artisan would have an understanding that the ingredients of Noda and those of Broh-Kahn would be incompatible since Noda's composition is for external administration, and Broh-Kahn's composition is for absorption through the oral mucosa. For the foregoing reasons, Applicants submit that the claims are not obvious over the cited references and respectfully request that the rejection be withdrawn.

C. U.S. Patent No. 3,257,276 to Broh-Kahn et al. in view of U.S. Patent No. 5,736,574 to Burnier et al. and U.S. Patent No. 5,965,610 to Modak et al. as evidenced by U.S. Patent No. 4,870,108 to Page

Claims 2-5, 8, 9, 10 and 33 stand rejected under 35 U.S.C. § 103(a) as obvious over Broh-Kahn in view of Burnier and further in view of U.S. Patent No. 5,965,610 to Modak et al. (hereafter, "Modak") as evidenced by Page. The Examiner contends that the combined disclosure of Broh-Kahn and Burnier describes a composition comprising benzalkonium chloride, a gelling agent, alcohol and octoxyglycerin. The Examiner further alleges that Modak describes a gel comprising emulsifiers, thickening agents, silicone polymers and other ingredients. According to the Examiner, it would have been obvious to combine Modak's emulsifiers, thickening agents and silicone polymers with the composition defined by the combined disclosure of Broh-Kahn and Burnier to create the claimed invention.

Applicants respectfully disagree. As previously discussed, an artisan of ordinary skill, in view of Broh-Kahn and Burnier, would have no reasonable expectation that the ingredients of Broh-Kahn and Burnier could be successfully combined into a single composition, as encompassed by the claims. Applicants submit that Modak merely provides emulsifiers, thickening agents and silicone polymers that can be included in a gel composition. Modak does not cure the deficiencies of Broh-Kahn and Burnier in describing the claimed invention, and as such, combining the disclosure of Modak with those of Broh-Kahn and Burnier does not render the claims obvious. In view of the foregoing, Applicants submit that the claims are not obvious over the cited references and respectfully request that the rejection be withdrawn.

III. The Double Patenting rejection

Claims 1, 2, 3, 5, 7-10, 12, 13, 16, 19, 20, and 22 stand provisionally rejected for nonstatutory obviousness-type double patenting over claims 1, 3-11, and 17 of co-pending application serial no. 10/622,272 (hereafter “the ‘272 application”). According to the Examiner, it would have been obvious to combine the ingredients noted in the ‘272 application to arrive at the presently claimed invention.

Since the rejection is provisional because the allegedly overlapping claims have not yet been patented, to the extent that claim scope overlaps in any patented case, Applicants respectfully submit that the appropriate action will be taken as the Examiner indicates allowable subject matter with regard to the pending rejections under 35 U.S.C. § 103(a).

IV. Conclusion

In view of the above remarks, it is respectfully requested that the application be allowed and passed to issue. If there are any other issues remaining which the Examiner believes could be resolved through either a Supplemental Response or an Examiner's Amendment, the Examiner is respectfully requested to contact the undersigned at the telephone number indicated below. Applicants believe that no fee is due at this time. However, if any fee is required, the Commissioner is authorized to charge such fee to Deposit Account No. 02-4377.

Respectfully submitted,
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Dated: 11/2/2009


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